

## Medicines and supportive strategies for the management of epilepsy in the mid and later stages of juvenile CLN3 (Batten) disease

*Please note: the information contained in this document is intended to provide supportive guidance to families, carers and associated professionals. It is not intended to be, nor is it, medical advice for individual children or adults with juvenile CLN3 (Batten) disease. Parents and carers should consult the person's GP prior to changing medication, medical treatment or prescribed activities. If you are a professional and you require more information, in the first instance please contact Sarah Kenrick (contact details at end), who can provide you with a link to the Adult Neurology Consultant for Heather House and/or the GP for Heather House.*

**Juvenile CLN3 (Batten) disease** is a very rare neurodegenerative disease.

**SeeAbility's Heather House** opened in July 1999 specifically to provide long term and palliative care and support for people with juvenile CLN3 (Batten) disease. Since then we have supported 30 younger adults with juvenile CLN3 (Batten) disease aged between 16 and 32.

Over the past 20 years we have been able to gather data to inform our management of seizures in the mid to later stages of the disease, always striving for the best possible outcomes for each individual. This work to enable people to take control of their lives and minimise the episodes of seizure activity has been at the forefront of our work.

In 2013 Heather House was able to collate evidence gathered over 9 years and present accumulated data on epilepsy in juvenile CLN3 (Batten) disease, thanks to funding from the BDFA (Batten Disease Family Association) flexible small grants scheme. From this we were able to give a presentation at the BDFA conference in 2014: 'Understanding epilepsy and best practice for young adults with juvenile CLN3 (Batten) disease'.

### Background Information

As well as developing our scope of practice with epilepsy, we have also been able to understand how other areas of skill and/or function loss affect each person with juvenile CLN3 (Batten) disease in different ways, and how some individuals with a compromised ability to communicate can be affected by a number of factors which can cause such a stressful situation for the person that their behaviour may give the appearance of an increase in seizures. This is particularly evident, in our experience, in relation to incontinence, mobility, gastric reflux and spatial awareness which have been alluded to briefly here and will be expanded on in separate documents.

For instance, our collective data shows us that an individual who is by nature 'anxious' will normally have more seizures and more types of seizures, particularly if they present as non-ambulant between 15-17 years of age. So much of our work with this type of person is our ability to understand the triggers, the fears and what helps keep the person grounded. This gives the potential to be more conservative with medicine doses and develop strong support techniques.

We have seen in the past 10 years a reduction in the instances of seizure activity across the group. As a collective at present we see an average of 1-3 tonic-clonic seizures a month and 4-6 partial seizures for the whole group. Individually half of our current group have less than 1 seizure every 3 months and this is across the age range above.

We assess the mental capacity of all people living at Heather House, according to their need and specific issues. Once someone is unable to retain information and communicate effectively, they are generally assessed as not having capacity and best interests decision making processes are employed for all treatment or invasive procedures.

We collect data around basic observations of pulse, temperature, respiratory rate, blood pressure and oxygen saturation levels. We do this monthly for people who are ambulant or can stand for transfers and eat orally. We do this weekly when the person can no longer stand and is reliant on enteral nutrition for some of the day. The benefit of these relatively simple and non-invasive procedures is the development of 'predictability' scores that enable us to identify problems with heart conductivity, changes prior to chest infection and with periods of weakness that affect breathing.

We have been able to identify how the presentation of early heart conductivity problems is easy to misdiagnose as hallucinations or epilepsy. For the person to feel something is wrong and not be able to communicate this feeling effectively must be truly terrifying. However, taking and recording the person's pulse on the same day and same time just once a week every week enabled us to present a clear record of a gradually slowing heartbeat. This could then be investigated by a cardiologist, leading to the individuals concerned to be fitted with pacemakers.

Another area that we have identified as often leading to perceived increased epilepsy is the onset of urinary and faecal incontinence and specifically when the person is unable to control continence and has a feeling of being 'wet'. The way the person may show this distress can be similar to how they may present when having focal seizure activity. This potentially leads to an increase in seizure medicines. Whilst some people have no issue with the transition to wearing adult pads, others find this very difficult to cope with.

## Seizures

**As the disease progresses**, for most people we see an increase in focal seizure activity and partial seizure activity. The tonic-clonic seizures are often less problematic. For some people we see no real change in seizure type or pattern.

**Below are some medicines we have found to be more or less effective, however please speak to the person's GP or consultant for appropriate medical advice.**

### Medicines we have found effective are:

- **Sodium valproate** – Has proven to be the most used and effective monotherapy for all seizure types and also used in conjunction with other anticonvulsants for complex seizure patterns.
- **Lamotrigine** – Used in smaller doses in conjunction with sodium valproate to manage escalation in all seizure types once the therapeutic dose of valproate is reached.
- **Phenobarbital** – Introduced when the person is having an increasingly complex seizure pattern and when individual seizures are prolonged or lead to clusters, this is normally

when the person is older (above 20 years) and no longer able to walk or bear weight. It is used normally in conjunction with the medicines above in small doses and appears to suit the disease profile well. We do not see a marked increase in drowsiness compared to that already experienced at this stage of the disease. Phenobarbital is used for all types of seizures, from tonic-clonic seizures to partial and focal seizures. Phenobarbital is often overlooked as it can cause long term health issues and drowsiness in the broader population. In juvenile CLN3 (Batten) disease increased sleepiness in the mid to later stages is very common. For people that have started phenobarbital early as monotherapy rather than valproate, we have seen far less types of seizure and much less agitation and very few and in one case no further anticonvulsants were needed as additional therapy.

- **Lorazepam** – Used in small doses only when there is a spike in focal seizures, partial seizures, panic and anxiety, it can be used both as required and regularly. We have not seen particular dependence on this drug, we have been able to withdraw and titrate doses quite easily.

### Other medicines we use for epilepsy are:

- **Levetiracetam** – Has some efficacy for tonic-clonic seizures but when used as monotherapy we see it is less effective as the person ages. We have also seen an increase in irritability and mood swings in some cases.
- **Clonazepam** – We use it for partial seizures and focal seizures in conjunction with other medication in the later stages, however is quite sedative.
- **Clobazam** – Has proved effective for some focal and partial seizures as above.

### Medications we have found less effective are:

- **Topiramate** – In the majority of cases it was observed to slow down thought process, causing difficulties in concentration, speech, oral eating and drinking skills, fine motor movement and mobility. When doses were reduced or withdrawn in favour of other anticonvulsants, these skills returned but not always to the previous level. It was also observed that seizures increased when topiramate was used, but reduced when withdrawn. In 20 years there were three cases of people moving to Heather House having been prescribed topiramate for some years. In these cases the individuals had complex presentations with other co-morbidities. When we tried to reduce topiramate, the individuals experienced aggressive and unstable epilepsy patterns, so doses were reinstated.
- **Phenytoin** – Is useful in acute situations where seizures are so unstable that they lead to emergency hospital admission, however for longer term therapy phenobarbitone works as well, but without the side effects of gum hypertrophy.

### Rescue medicines:

For younger people who remain ambulant, buccal midazolam is the safest and most effective rescue medicine.

Once people become older (19 years and above), there may be an increase in the complexity of seizures. As the person loses skills there is an element of confusion and agitation at times, which can present almost as seizure activity. For more complex epilepsy, firstly it is important to ascertain that

the person is still able to eat and drink orally and take medicines orally. What we have found is as these skills decrease, the ability to take medicine orally is less consistent. Anxiety of not being able to give/take medicines that is experienced by both the parent or carer and the person can cause much of this agitation and anxiety. This causes an increase or fluctuating pattern of seizure activity, so thinking about alternative nutrition methods (Percutaneous Endoscopic Gastrostomy or PEG) and having this in place early enough can lessen the need for rescue medicines, as well as the need for increased regular medicines. So we can look at a PEG as a device that enables us to support the person with their epilepsy more effectively.

All of the people with juvenile CLN3 (Batten) disease living at Heather House are supported to make their own decision, or be involved in the decision (depending on capacity at the time) to have a gastrostomy device fitted. We have seen that enabling individuals to identify the benefits of a gastrostomy device to help with medicines, on days when they are less in control or days when they have seizure, gives them a sense of safety and reduces anxiety around "will I be able to eat/swallow today?".

For adults (over 21) we have found that generally the episodes of status epilepsy or cluster seizures where we do need to use a rescue medicine are infrequent (twice a year or less). Often buccal midazolam is not effective or is seen to cause a drop in pulse and respiration. If this is seen then we give diazepam or lorazepam via PEG and for cases of status epilepsy, where there is a cyclical pattern of panic, partial seizure and tonic-clonic seizure in rapid succession that becomes repetitive, we use rectal paraldehyde. If necessary this dose is repeated after 20 minutes. Rectal paraldehyde is not readily available and is costly, but it proves very useful for the most complex and rapidly recurring cases of status epilepsy in juvenile CLN3 (Batten) disease. This pattern of cyclical and recurring epilepsy is most often seen in adults who are in the mid to late stages of the disease process or where there is underlying infection present.

Most important when using rescue medicine is to know when to use it and to use it promptly once the thresholds have been established. If a person suddenly presents with status and they have been stable previously we would always check if a urine infection or ear infection is present and whether they have had difficulty opening their bowels, as these can cause an increase in epilepsy in juvenile CLN3 (Batten) disease.

## **Oesophageal reflux and digestive transit**

We see every person develop reflux as they become less mobile and more dependent on a wheelchair. As they lose tone and muscle strength we also see that transit of food slows, and in the later stages can become intermittent. Reflux pain in a person who struggles to communicate and interpret what is happening can lead to panic and sweating, often being misinterpreted as epileptic activity, so good management of reflux is essential for the persons comfort and to aid better understanding of the person's seizure pattern.

So all people who have a PEG are prescribed a variant of omeprazole, Gaviscon after meals to prevent reflux pain and, if necessary, domperidone to aid gut transit. Postural management is also important to reduce reflux.

## **Epilepsy support is person centred**

The medicines prescribed by the consultant or GP treat the person's epilepsy, but what we have identified over the years is that we cannot stop the epilepsy completely or forever, nor can we prevent it from changing, sometimes escalating. Through science we are learning more about the protein deficiency that causes juvenile CLN3 (Batten) disease. We have seen some people experience few seizures, others many and complex seizures. We have long thought that people may have differing amounts of this protein present, which is why we see different seizure patterns for each person.

We have learned from so many inspiring people with juvenile CLN3 (Batten) disease that supporting a person's day to day to have minimal stress, their own routine, and family members and care givers who understand what is important to that person makes a big difference to how the person can be in control and feel safe. We have to keep in mind that the things we may feel important are not necessarily important to the person. We have seen that acceptance, embracing the ordinary and celebrating the extraordinary achievements for people is the key to balance, which in turn can enable not only seizure management but symptom management on a wider scale.

For more information, advice or support please contact

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